APPENDIX 4

Investigator's Handbook

Section 15

Accountability and Storage of Investigational Drugs

(http://ctep.info.nih.gov/handbook/handbook/default.htm)

15. Accountability and Storage of Investigational Agents

The investigator is responsible for the proper and secure physical storage and recordkeeping of investigational agents received from CTEP. Specifically, the investigator must:

- Maintain a careful record of the receipt, use, and final disposition of all investigational agents received from CTEP, using the NCI Drug Accountability Record Form (DARF) (Appendix XIII)
- Store the agent in a secure location, accessible to only authorized personnel, preferably in the pharmacy
- Maintain appropriate storage of the investigational agent to ensure the stability and integrity of the agent
- Return any unused investigational agents to PMB at the completion of the study or upon notification that an agent is being withdrawn.

The intent of the drug accountability procedures described in this section is to assist the investigator in making certain that agents received from DCTD are used only for patients entered onto an approved protocol. The recordkeeping described in this section is required under FDA regulation. Investigators are responsible for the use of investigational agents shipped in their name. Even if a pharmacist or chemotherapy nurse has the actual task of handling these agents upon receipt, the investigator is the responsible individual and has agreed to accept this responsibility by signing the FDA 1572.

15.1 Procedures for Drug Accountability and Storage

- Each investigational agent should be stored separately by protocol. If an agent is used for more than one protocol, there should be separate physical storage for each protocol. Remember that CTEP provides and accounts for agents on a protocol-by-protocol basis.
- Each agent should be accounted for separately by protocol. If an agent is used for more than one protocol, there should be a separate Drug Accountability Record Form (DARF) for each protocol (Appendix XIII). There should be a separate DARF for each agent in a multi-agent protocol.
- Separate accountability forms should be maintained for each different strength or dosage form of a particular agent (e.g., an agent with a 1-mg vial and a 5-mg vial would require a different DARF for the 1-mg vial than for the 5-mg vial).
- The DARF has been designed for use at each location where agents are stored, e.g., main pharmacy, satellite pharmacy, physician's office, or other dispensing areas.
- The DARF is also designed to accommodate both dispensing records and other agent transaction documentation (e.g., receipt of agent, returns, broken vials, etc.). A copy of the DARF may be found in Appendix XIII.
- DCTD-supplied investigational agents may be transferred, with an institutional (intra-institutional transfer) from a completed DCTD protocol to another DCTD-approved protocol that utilizes the same agent and formulation. An NCI Investigational Drug Transfer form must be completed and submitted by fax (301-402-0429) to the Pharmaceutical Management Branch for each agent transfer. Transfer forms should be submitted within 72 hours of the actual transfer. Transfer of DCTD-supplied investigational agents from an active protocol requires prior PMB approval (telephone 301-496-5725). (See PMB Policy and Guideline on the CTEP Home Page.)
- Inter-institutional transfer of DCTD investigational agents is not permitted unless specifically approved or authorized by the Pharmaceutical Management Branch.

15.2 Investigational Agent Returns

Many investigators are not aware that investigational agents must be returned to the IND sponsor. DCTD, as the investigational agent sponsor, is responsible for investigational agent accountability, which includes receipt, distribution, and final disposition of all investigational agents. Investigators are required to return agents if:

- The study is completed or discontinued
- The agent is expired
- The agent is damaged or unfit for use (e.g., loss of refrigeration).

In situations where a DCTD agent is no longer required for a completed or discontinued protocol, DCTD procedures permit the transfer to another DCTD-sponsored protocol that is using the identical agent and formulation through completion of the NCI Transfer Investigational Drug Form, NIH-2564, see Section 15.1 (Appendix XIII).

In situations where there is an obvious excess inventory, or the agent will not be used before the expiration date and you have another DCTD protocol(s) using the identical agent, please contact the Pharmaceutical Management Branch (301-496-5725) for assistance in transferring the agent to another DCTD-sponsored study. Otherwise, return the agents as stated in the steps below.

To return investigational agents to DCTD:

(1) Package the agents securely to prevent breakage (enclose within a zip-lock bag where appropriate).

(2) Complete the Return Drug List Form, NIH-986 (Appendix XI).
(3) Send to the Clinical Drug Repository at the address indicated on the Return Drug Form. Because agents are not re-used upon return, rush delivery is not necessary.

15.3 Verification of Compliance

Investigators are reminded that compliance with procedures to ensure proper agent usage will be reviewed during site visits conducted under the monitoring program. Specifically, site visitors will check that the drug accountability system is being maintained and will spot-check the drug accountability records by comparing them with the patients' medical records to verify that the agents were administered to a patient entered in the recorded protocol.

15.4 Handling of Antineoplastic Agents

There has been considerable concern about the potential risk of chronic exposure to low-level concentrations of antineoplastic agents among health care workers routinely handling these agents. The potential mutagenic activity of antineoplastic agents has been examined *in vitro* and *in vivo*. Urinary alkylating and anthracycline agents have shown mutagenic activity in experimental systems, whereas this has not been demonstrated for most of the antimetabolites and vinca alkaloids. Recent reports indicate that antineoplastic agents may be absorbed by workers who are handling them. In addition, some of the compounds are carcinogenic in animals and are suspected of being so in humans, but only in patients receiving the agent at therapeutic levels.

There is, however, no clear evidence at this time that chronic exposure to low-level concentrations of antineoplastic agents has been carcinogenic in health-care workers. Nevertheless, it would seem prudent to consider the adoption of certain precautions in the procedures of workers handling these agents.

Several professional organizations have reviewed the data on this subject in an attempt to develop guidelines for safe handling. While there are now several published sets of guidelines, they do not differ significantly.

We have reproduced the *Recommendations for Handling Cytotoxic Agents,* by the National Study Commission on Cytotoxic Exposure in Appendix XIV. Please not that these are guidelines and do not have regulatory or legal force. They are included for your consideration and information.

Other pertinent references include:

- Recommendations for the Safe Handling of Parenteral Antineoplastic Drugs. NIH Publication #83-2621. Available from Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.
- ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. *Am J. Hosp. Pharm.* 1990; 47:1033-1049.
- AMA Council Report: Guidelines for Handling Parenteral Antineoplastics. JAMA 1985; 253:1590-1592.

Form approved:
OMB No. 0925-0240
Expires: 1/31/2001

National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

PAGE NO.
CONTROL RECORD ☐
SATELLITE RECORD ☐

Investigational Agent Accountability Record

Name of Institution:	NCI Protocol No.:
Agent Name:	Dose Form and Strength:
Protocol Title:	Dispensing Area:
Investigator Name:	NCI Investigator No.:

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials
1.								
2.								
3.								
4.								
5.								
6.								
7.								
8.								
9.								
10.								
11.								
12.								
13.								
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24.								

Form approved:
OMB No. 0925-0240
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National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

Transfer Investigational Agent Form

Investigational Agent Accountability

Investigator transferring agent:*	NCI Investigator No.:	Date of transfer:
Dr.		

Name of Institution:

Street Address:	City:	State:	Zip Code:

This form is to be used for intra-institutional transfer(s) only for the following reasons. (*Please check one of the boxes below.*)

☐ Completed Protocol ☐ Unused Agent Obtained for Special Exception Protocol

The following agent(s) required for NCI-approved protocol(s) are being transferred to NCI-approved protocol(s) for:

Dr. _____ _____

Investigator receiving agent* NCI Investigator No.

Received on NCI Protocol No. **	Transferred to NCI Protocol No.	NSC No.	Agent Name	Strength and Formulation	Quantity	Manufacturer and Lot No.

Authorized Signature (Investigator or Designee)

Phone No.

Return form to:
Pharmaceutical Management Branch
Investigational Drug Branch
Division of Cancer Treatment and Diagnosis, NCI, NIH
Executive Plaza North, Room 707A
Bethesda, MD 20892

*Use one form per set of investigators.

** No additional agents will be supplied for this protocol number.

All requested information MUST be supplied for form to be valid.

NIH-986 (REV. 2/97)

12/00

National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

Return Drug List

Return only agents supplied by the National Cancer Institute

The agents listed below were ordered by (one investigator per form only):

Dr.

NCI Investigator No.:

Address: (Including Institution)

☐ **Check here if returned receipt should be mailed to the above address, OR fill in a fax number below**

FOR NCI USE ONLY

Return. No.:

Signature of Authorizing Official:

Date of Authorization:

	NSC Number	Agent Name	NCI Protocol Number	Strength, Unit, & Dose (Specify vials, capsules, or tablets)	Lot Number (or Patient ID for Blinded Trial)	Manufacturer	Quantity (Specify whole or partial containers)	Container Number	Action
1									
	Reason for return: ☐ Agent expired ☐ All patient(s) off treatment. ☐ Protocol complete ☐ Other:								
2									
	Reason for return: ☐ Agent expired ☐ All patient(s) off treatment. ☐ Protocol complete ☐ Other:								
3									
	Reason for return: ☐ Agent expired ☐ All patient(s) off treatment. ☐ Protocol complete ☐ Other:								
4									
	Reason for return: ☐ Agent expired ☐ All patient(s) off treatment. ☐ Protocol complete ☐ Other:								
5									
	Reason for return: ☐ Agent expired ☐ All patient(s) off treatment. ☐ Protocol complete ☐ Other:								
6									
	Reason for return: ☐ Agent expired ☐ All patient(s) off treatment. ☐ Protocol complete ☐ Other:								

Date Received:

INSTRUCTIONS:

1. Properly complete all sections to receive credit for the return.
2. Type all information-one item, lot, or protocol per line.
3. DO NOT mark in shaded areas.
4. Investigator signature or signature of individual preparing this form:

Signature / Printed Name *Date*

Title *Phone No.*

5. Pack the agent(s) well to minimize breakage and leakage.
6. All agents may be returned via room temperature shipment.
7. Enclose the completed list with the agent(s) and return to:

NCI Clinical Repository
627 Lofstrand Lane
Rockville, MD 20850
Attn: Returns

RETURN RECEIPT: To obtain a return receipt by fax, provide your number in the space below.

CLINICAL DRUG REQUEST

PHARMACEUTICAL MANAGEMENT BRANCH
CANCER THERAPY EVALUATION PROGRAM
DIVISION OF CANCER TREATMENT AND DIAGNOSIS
NATIONAL CANCER INSTITUTE, NIH

Return by FAX to:
Drug Management and Authorization Section (301) 480-4612

The drugs listed below are requested for the use of (please type or print):

Dr. _____ NCI Investigator Number: _____

Designee/Requester (if other than investigator) (please type or print):

Name _____ Title: _____

Telephone Number: _____ FAX Number: _____

Return by U.S. Mail to:
Pharmaceutical Mgt. Branch
Drug Mgt. & Authorization Section
Division of Cancer Treatment and Diagnosis, NCI
Executive Plaza North, Room 707
9000 Rockville Pike
Bethesda, MD 20892-7422 U.S.A.

Return by Express Courier to:
Pharmaceutical Mgt. Branch
Drug Mgt. & Authorization Section
Division of Cancer Treatment and Diagnosis, NCI
Executive Plaza North, Room 707
6130 Executive Blvd.
Rockville, MD 20852 U.S.A.

_____
Investigator/Designee Signature **Date**

COMMENTS:

	NCI Protocol Number	No. of Pts. Currently Being Treated	Patient or Special Code (if applicable)	Your Current Inventory	NSC Number	Drug Name	Strength & Dosage Form (Specify vials, tablets, etc.)	Quantity Ordered (Specify vials, bottles, etc.)	Date Needed
A									
B									
C									
D									
E									

SHIPPING ADDRESS:

MISCELLANEOUS: Urgent shipments must be accompanied by an express courier account number.

Express Courier Name: _____

Express Courier Acct. No.: __ __ __ __-__ __ __ __-__

Reference No.: _____

Express Courier Acct. No.(if other format): _____

INSTRUCTIONS:

1. TYPE ALL INFORMATION - One item or protocol per line.
2. Order using NCI protocol numbers only. Local protocol numbers will cause a delay.
3. Fill in all sections completely including the official shipping address.
4. Limit drug request to an eight (8) week supply.
5. Sign and date the order (must be investigator or designee signature only).
6. Do not mark box labeled FOR NCI USE ONLY.
7. Return to DMAS (see above).